The Examiner has rejected claims 1-35 and 37 under 35 USC §112 as allegedly containing subject matter which was not described in the specification in such a way as to enable one of skill in the art to which it pertains to make and/or use the invention. The crux of the Examiner's rejection is that Applicants have not demonstrated that the specification enables making and using any and all transgenic animals of the type claimed, wherein the animal expresses an epitope-tagged TBP at a level sufficient to allow for the isolation of TBP-containing complexes. On page 3 of Paper 12 (11/5/99 Office Action), the Examiner acknowledges that Applicants have demonstrated "that the transgenic hTBP was expressed in the transgenic mice at the protein level," but asserts that Applicants have not shown "that the level of expression was sufficient to permit isolation of hTBP-containing complexes." Further on the same page, the Examiner acknowledges that Applicants have demonstrated the "purification of epitope-tagged TBP from nuclear extracts of liver, brain, and kidney tissue," but asserts that purification of the hTBP-containing complexes is not described. The Examiner further asserted, with regard to claims 26-35, that competition with murine TBP may prevent hTBP from forming enough complex to permit isolation of hTBP-containing complexes, and that this uncertainty also rendered the claims non-enabled.

A §1.132 Declaration was filed concurrently with this set of Supplemental Remarks. The Declaration enclosed includes post-filing data in the form of several Western Blot gels and statements by Dr. Kirschbaum that the gels demonstrate that using the methods disclosed in the specification as well as techniques well known in the art at the time of the invention, the Applicants were, in fact, able to demonstrate that the level of expression of hTBP was sufficient to permit isolation and purification of hTBP-containing complexes. The methods of processing tissue samples for nuclear extract preparation, electrophoresis and transfer of purified protein samples, Western Blot analysis, immunodetection of selected TAFs using monoclonal antibodies and alkaline phosphatase conjugated secondary antibodies were all carried out under standard

conditions in accordance with the methods described in Dr. Berglund's thesis, of record, in sections 3.2.2.10. through 3.2.3.5 (pages 38 to 46).

On page 4 of Paper 12, the Examiner acknowledges that the Applicants have described transcription assays wherein epitope-tagged hTBP was shown to activate transcription. The Examiner asserts however, that while the Applicants have concluded that the fractions tested exhibited TFIID activity, that "there is nothing to indicate that anything other than hTBP alone was responsible for the activation of transcription." Applicants respectfully disagree. On page 61 of his Thesis, Dr. Berglund states..."the ability of such regulatory factors to activate transcription is dependant on the presence of certain TAFII subunits in the holo-TFIID. It has been reported that the TBP subunit alone can not support activated transcription in vitro." In support of this statement, Dr. Berglund cites four prior art references[1]. In addition, two other references, also cited in Dr. Berglund's thesis, further support this statement.[2,3] In the 1993 publication (footnote 3), Zhou et al conclude that "the TAFs associated with TBP in TFIID are required for transcriptional activation by activator proteins." Thus, in Dr. Berglund's thesis alone, Applicants have put forth six references that indicate that TBP alone could not have been responsible for the activation of transcription. These references, in addition to the evidence put forth in the accompanying Declaration, demonstrate that Applicants have provided adequate guidance for preparing a transgenic animal that expresses the epitope-tagged TBP at a level sufficient to allow for the isolation of TBP-containing complexes.

[1] Pugh, B.F. and R. Tjian. 1990. Mechanism of transcriptional activation by Sp1: evidence for coactivators. *Cell* 61:1187-1197; Hoey, T., B.D. Dynlacht, M.G. Peterson, B.F. Pugh and R. Tjian. 1990. Isolation and characterization of the Drosophila gene encoding the TATA box binding protein, TFIID. *Cell* 61: 1179-1186; Dynlacht, B.D., T. Hoey, and R. Tjian. 1991. Isolation of coactivators associated with the TATA-binding protein that mediate transcriptional activation. *Cell* 66:563-576; and Tanese, N., B.F. Pugh, and R. Tjian. 1991. Coactivators for a proline-rich activator purified from the multisubunit human TFIID complex. *Genes and Development* 5:2212-2224.

[2] Zhou, Q., P.M. Lieberman, T.G. Boyer, and A.J. Berk. 1992. Holo-TFIID supports transcriptional stimulation by diverse activators and from a TATA-less promoter. *Genes and Development* 6:1964-1974.

[3] Zhou, Q., T.G. Boyer, and A.J. Berk. 1993. Factors (TAFs) required for activated transcription interact with TATA box-binding protein conserved core domain. *Genes and Development* 7:180-187.

In light of the comments above as well as the Declaration filed herewith, Applicants respectfully request removal of all rejections and allowance of all pending claims.

A first office action on the merits is awaited. Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date: March 15, 2002

Heller Ehrman White & McAuliffe LLP
1666 K Street, N.W., Suite 300
Washington, D.C. 20006-4004
Telephone: (202) 912-2000
Facsimile: (202) 912-2020

Patricia D. Granados
Reg. No.: 33,683

Customer No. 26633